REMARKS

The present Amendment is in response to the Examiner's Office Action mailed on June 16, 2003. Claims 22, 24 and 26-53 have been cancelled. Claims 1-21 and 25 have been amended. Claims 1-21, 23 and 25 are pending.

Reconsideration of the application is respectfully requested in view of the above amendments to the claims and the following remarks. For the Examiner's convenience and reference, Applicants' remakes are presented in the order in which the corresponding issues were raised in the Office Action.

I. Rejections Under 35 U.S.C. §112, First Paragraph

The Examiner rejects claims 1-20, 23-47 and 51-53 under 35 U.S.C. §112, first paragraph for lack of enablement. Specifically, the Examiner alleges that the specification, while being enabling for 5-fluorouracil, does not reasonably provide enablement for every pyrimidine base analog. Applicants' amendment to the pending claims renders the rejection moot.

The Examiner also rejects claims 1-53 under 35 U.S.C. §112, first paragraph for failing to comply with the written description requirement. Specifically, the Examiner alleges that the compound 5-fluorouracil would not adequately represent the genus of the pyrimidine base analog for treating cancer broadly. Applicants' amendment to the pending claims renders the rejection moot.

II. Rejections Under 35 U.S.C. §112, Second Paragraph

The Examiner rejects claims 1-20, 23-47 and 51-53 under 35 U.S.C. §112, second paragraph for being indefinite because of the absence of the specific analogs to the chemical core claimed (CCC) or distinct language to describe the structural modifications or the chemical name(s) of derivatized of the invention. Applicants' amendment to the pending claims renders the rejection moot.

III. Rejection Under 35 U.S.C. § 103(a)

The Examiner rejects claims 1-53 under 35 U.S.C. §103(a) as being unpatentable over Rubinfeld (US Patent No: 6,191,119) in view of Achterrath (US Patent No: 6,403,569).

Independent claim 1 as amended specifies a method for treating a cancer patient by using a sequential therapy of a 20(S)-camptothecin and 5-fluorouracil. Specifically, the sequential therapy involves the following 2 steps:

1) administering 5-fluorouracil to the patient; and

2) administering to the patient a 20(S)-camptothecin at least 1 day before or after 5-fluorouracil is administered to the patient.

In contrast, Rubinfeld discloses using 20(S)-camptothecin in combination with other therapeutics in general. As acknowledged by the Examiner, Rubinfeld discloses that 20(S)-camptothecin and the other therapeutics can be co-administered during **overlapping** periods of time. Nowhere in this reference is there a teaching or suggestion that a 20(S)-camptothecin and 5-fluorouracil are administered **sequentially** by following the regimen specified in claim 1.

On the other hand, Achterrath merely teaches a combination therapy of camptothecin (e.g., CPT-11), 5-fluorouracil (5-FU), and folinic acid (FA). According to Achterrath, a **combination of these three agents** is administered, e.g., by infusion weekly, or in by following the de Gramont treatment schedule, in which is combination is administered in two-week intervals. Column 3, lines 49-62. As demonstrated by Achterrath,

> **On day 1,** FA 200 mg/m^2 i.v. was administered over **2 hours followed by** the administration of 400 mg/m^2 5-FU i.v. bolus and 600 mg/m^2 5-FU i.v. over **22 hours** (one cycle) and administration of 180 mg/m^2 CPT-11 i.v. **On day 2,** 200 mg/m^2 i.v. of FA was administered over 2 hours.

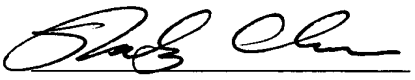
Column 5, lines 23-28. Emphasis Added. Clearly, Achterrath teaches a combination therapy with a dosing regimen of co-administration of CPT-11, 5-FU and FA **within a day**. Achterrath neither teaches nor suggests the claimed sequential therapy requiring the 20(S)-camptothecin be administered at least 1 day before or after the administration of 5-FU.

In view of the failure of the cited references to teach or suggest all of the claim limitations, a prima facie case of obviousness has not been established. Withdrawal of the rejection under 35 U.S.C. §103(a) is therefore respectfully requested.

CONCLUSION

Applicants believe that they are entitled to a letters patent, and respectfully solicit the Examiner to expedite prosecution of this patent to issuance. Should the Examiner have any questions, Examiner is encouraged to telephone the undersigned.

Respectfully submitted,

Date: Oct. 16, 2003 By: 

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